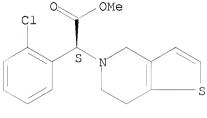
RN 120202-66-6 REGISTRY
ED Entered STN: 21 Apr 1989
CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α-(2-chlorophenyl)-6,7-dihydro-, methyl ester, (αS)-, sulfate (1:1) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α-(2-chlorophenyl)-6,7-dihydro-, methyl ester, (S)-, sulfate (1:1)
OTHER NAMES:
CN (S)-(+)-Clopidogrel hydrogensulfate
CN (S)-(+)-Methyl (2-chlorophenyl)(6,7-dihydro-4H-thieno[3,2-c]pyrid-5-yl)acetate bisulfate
CN (S)-(+)-Methyl 2-(2-chlorophenyl)-2-(6,7-dihydro-4H-thieno[3,2-c]pyridin-5-yl)acetate hydrogen sulfate
CN Clopidogrel bisulfate
CN Clopidogrel hemisulfate
CN Clopidogrel hydrogen sulfate
CN Iscover
CN Methyl (S)-(4,5,6,7-tetrahydrothieno[3,2-c]pyridin-5-yl)(2-chlorophenyl)ethanoate hydrogen sulfate
CN Plavix
CN SR 25990C
FS STEREOSEARCH
MF C16 H16 Cl N O2 S . H2 O4 S
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, EMBASE, HSDB*, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, PATDPASPC, PROMT, PROUSDDR, PS, SCISEARCH, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)

CM 1

CRN 113665-84-2
CMF C16 H16 Cl N O2 S

Absolute stereochemistry. Rotation (+).



CM 2

CRN 7664-93-9
CMF H2 O4 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

227 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
232 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     7.61       7.82

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FILE LAST UPDATED: 30 Mar 2008  (20080330/ED)

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=> s l1 and (form I(l)form II)
            232 L1
        1704688 FORM
        4462888 I
           7200 FORM I
                  (FORM(W)I)
        1704688 FORM
        2211482 II
           4326 FORM II
                  (FORM(W)II)
           1786 FORM I(L)FORM II
L2            7 L1 AND (FORM I(L)FORM II)

=> d bib abs 1-7

L2   ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2008 ACS on STN
AN   2007:174397  CAPLUS
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DN 146:213027
TI Novel process for preparation of clopidogrel bisulfate polymorphic Form I
IN Kamath, Ajit; Mali, Subhash; Ranbhan, Kamlesh; Patil, Jotiba; Zunjarrao, Yuvraj
PA Arch Pharmalabs Limited, India
SO PCT Int. Appl., 13pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007017886	A1	20070215	WO 2005-IN287	20050811
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRAI WO 2005-IN287 20050811
AB Disclosed herein is an efficient and cost-effective process for preparation of stable (S)-(+)-clopidogrel polymorphic Form I without affecting the chiral purity by dissolving/suspending the (S)-(+)-clopidogrel bisulfate Form II in first organic solvent and precipitating using second organic solvent. The process is carried out at room temperature resulting in good yields and high purity. For example, 100 g of (S)-(+)-clopidogrel bisulfate Form II was dissolved in 400 mL of methanol at room temperature, methanol was distilled, the residue obtained was seeded with 2.2 g of (S)-(+)-clopidogrel bisulfate Form I and allowed to stir for 1 h. N-Bu acetate (800 mL) was added at room temperature to precipitate the solid. The solid was filtered, washed with Bu acetate and dried at room temperature to give 96.0 g of (S)-(+)-clopidogrel bisulfate Form I.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:101202 CAPLUS
DN 148:285078
TI Synthesis of crystalline forms I of clopidogrel hydrogen sulfate and mutual conversion of the crystalline forms
AU Pan, Xianhua; Mao, Haifang; Lang, Xihong
CS School of Biotechnology and Food Processing Engineering, Shanghai Institute of Technology, Shanghai, 200235, Peop. Rep. China
SO Jingxi Huagong (2006), 23(12), 1221-1226
CODEN: JIHUFJ; ISSN: 1003-5214
PB Jingxi Huagong Bianjibu
DT Journal
LA Chinese
AB A synthetic method for the production of crystalline form I of clopidogrel hydrogen sulfate (I) was improved. With 3-pentanone as solvent, a reaction at −10 to −16° for 10-16 h, gave I in 80%

yield. A method for the mutual conversion of the crystalline form I and crystalline form II of clopidogrel (II) was also developed. I and II were characterized by m.p., FTIR spectrometry and x-ray powder diffraction.

L2 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:193972 CAPLUS
DN 144:260838
TI Novel process for preparation of clopidogrel bisulfate polymorph
IN Sawant, Kamlesh Digambar; Tarur, Venkatasubramanian R.; Sathe, Dhananjay Govind
PA India
SO U.S. Pat. Appl. Publ., 7 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 20060047121	A1	20060302	US 2004-957891	20041004
	IN 2004MU00945	A	20070427	IN 2004-MU945	20040901
	US 20060074242	A1	20060406	US 2005-149646	20050610
PRAI	IN 2004-MU945	A	20040901		
	US 2004-957891	A2	20041004		
	WO 2005-IN48	A	20050215		

AB A process for making clopidogrel bisulfate Form I which comprises dissolving clopidogrel bisulfate Form II in a solubilizing solvent at room temperature to form a solution; adding an anti-solvent to the the solution till turbid; stirring the the turbid solution; collecting the precipitated solid and drying the final solid product, form I.

L2 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:612253 CAPLUS
DN 143:139168
TI Processes for preparation of different forms of (S)-(+)-clopidogrel bisulfate
IN Lohray, Braj Bhushan; Lohray, Vidya Bhushan; Pandey, Bipin; Dave, Mayank Ghanshyambhai; Dholakia, Parind Narendra
PA Cadila Healthcare Limited, India
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005063708	A2	20050714	WO 2004-IN341	20041102
	WO 2005063708	A3	20051006		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW		
	RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
	IN 2003MU01154	A	20060106	IN 2003-MU1154	20031103

	IN 2003MU01217	A	20060106	IN 2003-MU1217	20031125
	CA 2544443	A1	20050714	CA 2004-2544443	20041102
	EP 1680430	A2	20060719	EP 2004-820865	20041102
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU				
	NO 2006002062	A	20060724	NO 2006-2062	20060508
	KR 20070066779	A	20070111	KR 2006-710714	20060601
	US 20070082924	A1	20070412	US 2006-577940	20060712
PRAI	IN 2003-MU1154	A	20031103		
	IN 2003-MU1217	A	20031125		
	WO 2004-IN341	W	20041102		

AB The invention provides improved processes for the preparation of hydrated form of (S)-(+)-clopidogrel bisulfate as well as improved processes for the preparation of Form-I and Form-II of (S)-(+)-clopidogrel bisulfate. (S)-(+)-clopidogrel was dissolved in MeOH and treated with sulfuric acid to give a hydrated amorphous form.

L2 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:894728 CAPLUS
DN 142:204399
TI Qualitative and quantitative analysis of clopidogrel bisulphate polymorphs
AU Koradia, Vishal; Chawla, Garima; Bansal, Arvind K.
CS Department of Pharmaceutical Technology (Formulations), National Institute of Pharmaceutical Education and Research (NIPER), Punjab, 160 062, India
SO Acta Pharmaceutica (Zagreb, Croatia) (2004), 54(3), 193-204
CODEN: ACPHEE; ISSN: 1330-0075
PB Croatian Pharmaceutical Society
DT Journal
LA English
AB This study deals with characterization and quantification of form I and form II of clopidogrel bisulfate (CLP), a selective and irreversible inhibitor of ADP-induced platelet aggregation. Thermal (DSC, TGA, HSM), crystallog. (XRD) and spectroscopic (FTIR) methods were used for characterization. After characterization of active pharmaceutical ingredient (API), these techniques were further used for identification of the polymorphic form present in three marketed formulations (tablets). FTIR method was successfully developed and validated for the quantification of form I in polymorph mixts.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:950061 CAPLUS
DN 140:8764
TI Polymorphs of clopidogrel hydrogen sulfate
IN Lifshitz-Liron, Revital; Kovalevski-Ishai, Eti; Wizel, Shlomit; Avhar-Maydan, Sharon; Lidor-Hadas, Rami
PA Teva Pharmaceutical Industries, Ltd., Israel
SO U.S. Pat. Appl. Publ., 31 pp., Cont.-in-part of U.S. Ser. No. 74,409.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 20030225129	A1	20031204	US 2003-339008	20030108
	US 7074928	B2	20060711		
	US 20030114479	A1	20030619	US 2002-74409	20020212
	US 6767913	B2	20040727		

WO 2003051362 A2 20030626 WO 2002-US40679 20021218
WO 2003051362 A3 20030807
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2002-348182P P 20020111
US 2002-74409 A2 20020212
US 2002-359157P P 20020221
WO 2002-US40679 A 20021218
US 2001-342440P P 20011218
US 2001-342351P P 20011221

AB Provided are new crystalline Forms III, IV, V and VI of clopidogrel hydrogen sulfate and the amorphous form of clopidogrel hydrogen sulfate, as well as their pharmaceutical compns., and method of treatments with such compns. Also provided are novel processes for the preparation of clopidogrel hydrogen sulfate Form I, Form II, Form III, Form IV, Form V, Form VI and amorphous form. Clopidogrel base (4.27 g) was dissolved in Me Et ketone (MEK) (33.7 mL). Eighty percent aqueous H2SO4 (1.03 mL) was added to the solution at 20°. The reaction mixture was heated to reflux temperature for 2 h and then the solution was cooled to room temperature and stirred at this temperature for addnl. 67 h during which a precipitate was formed. The white solid was collected by filtration, washed with MEK and dried at 50° in a vacuum oven for 24 h to obtain 4.59 g (82%) of clopidogrel hydrogen sulfate crystal Form II.

L2 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:491043 CAPLUS
DN 139:74015
TI Polymorphs of clopidogrel hydrogen sulfate
IN Lifshitz-Liron, Revital; Kovalevski-Ishai, Eti; Wizel, Shlomit; Avhar-Maydan, Sharon; Lidor-Hadas, Rami
PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 2003051362 A2 20030626 WO 2002-US40679 20021218
WO 2003051362 A3 20030807
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	US 20030114479	A1	20030619	US 2002-74409	20020212
	US 6767913	B2	20040727		
	CA 2470479	A1	20030626	CA 2002-2470479	20021218
	AU 2002366383	A1	20030630	AU 2002-366383	20021218
	AU 2002366383	B2	20070614		
	EP 1467735	A2	20041020	EP 2002-805215	20021218
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	HU 2004002485	A2	20050428	HU 2004-2485	20021218
	JP 2005514387	T	20050519	JP 2003-552295	20021218
	US 20030225129	A1	20031204	US 2003-339008	20030108
	US 7074928	B2	20060711		
	ZA 2004004733	A	20050615	ZA 2004-4733	20040615
	IN 2004DN01705	A	20070323	IN 2004-DN1705	20040616
	MX 2004PA06088	A	20040927	MX 2004-PA6088	20040617
	NO 2004003038	A	20040909	NO 2004-3038	20040716
	IN 2007DN08318	A	20080111	IN 2007-DN8318	20071029
PRAI	US 2001-342440P	P	20011218		
	US 2001-342351P	P	20011221		
	US 2002-348182P	P	20020111		
	US 2002-74409	A	20020212		
	US 2002-359157P	P	20020221		
	WO 2002-US40679	W	20021218		
	IN 2004-DN1705	A3	20040616		

AB Provided are new crystalline Forms III, IV, V and VI of clopidogrel hydrogen sulfate and the amorphous form of clopidogrel hydrogen sulfate, as well as their pharmaceutical compns. for inhibiting platelet aggregation. Also provided are novel processes for preparation of clopidogrel hydrogen sulfate Form I, Form II, Form III, Form IV, Form V, Form VI and amorphous form. For example, 5.31 g of clopidogrel base was dissolved in 41.9 mL of Et acetate, and 1.29 mL of 80% aqueous H_2SO_4 was added. The reaction mixture was heated and a massive precipitate was formed; the solution was cooled to room temperature, and white solid was collected by filtration, washed with Et acetate and dried to obtain 4.60 g (66%) clopidogrel hydrogen sulfate Form II.